

REMARKS

The present invention relates to the use of civamide or one of its salts to provide long-lasting relief in the treatment of various painful disorders. The use of civamide as a medicament for painful disorders is known in the art, as shown, for example, in applicant's own prior U.S. 5,063,060, cited in the specification. The present invention is based on applicant's recent discovery that relatively short-term treatment with civamide can provide relatively long term relief, well after the short term treatment has been discontinued.

Claim 1 has been amended to more explicitly state the novel feature of the present inventive method. Claim 1 as amended now specifically states that the treatment continues for a relatively short term, the treatment is then discontinued, and the diminishment of pain continues for a relatively long period. This result is surprising and would not be expected in view of the prior art.

Claims 1-5 stand rejected under 35 U.S.C. § 112. Claim 1 is amended to delete the words "or prevention." Claims 3 and 5 are amended to recite the types of chronic pain amenable to treatment with intranasal and topical administration, respectively. It is believed that these amendments are sufficient to obviate the rejection.

The rejection of claims 1-5 under 35 U.S.C. § 102(b) is respectfully traversed. The cited reference, EP 0506658, is the European counterpart of applicant's own U.S. 5,063,060, which is cited and distinguished in the present specification. Nothing in these references teaches that civamide can be administered for a relatively short term, to provide surprisingly long-term relief after treatment is discontinued, as explicitly recited in claim 1. Accordingly, claim 1 is not anticipated. Claims 2-5, which depend on claim 1 either directly or indirectly, are not anticipated for the same reason.

The rejection of claims 1-5 under 35 U.S.C. § 103(a) in view of Brand also is respectfully traversed. Brand teaches the use of a capsaicinoid in combination with another analgesic compound to provide an analgesic effect. In his discussion of the prior art, Brand notes (p. 3, lines 13-16) that LaHann U.S. 4,313,958 discloses "[c]apsaicin (8-methyl-N-vanillyl-62-nonenamide) and 'synthetic' capsaicin (N-vanillyl-nonamide)" as analgesics. The "synthetic" capsaicin compound disclosed by LaHann and noted by Brand is not the same compound as civamide. Unlike civamide, the "synthetic" capsaicin is not a "cis" structure and does not have a methyl group in the -8 position.

The Examiner's confusion on this point is understandable, given the state of confusion in the literature regarding nomenclature of capsaicin and similar compounds. As noted in "Capsaicin: Identification, Nomenclature, and Pharmacotherapy," Cordell, et al., The Annals of Pharmacotherapy, March, 1993, Vol. 27, p. 330, 332:

"Substantial confusion has been introduced into both the chemical and biological literature by a compound that has erroneously been termed 'synthetic capsaicin.' This compound has the name N-[(4-hydroxy-3-methoxyphenyl)methyl]-nonanamide (Figure 4) . . . It is also known as pelargonic acid vanillylamide, and is officially named nonivamide.

"Structurally, nonivamide differs from capsaicin in two important ways. First, the double bond present in capsaicin has been reduced, and second, the methyl group on the fatty-acid chain has been removed . . . Because the structures of the two compounds are different, it is reasonable to expect that their biologic properties would also be quantitatively and qualitatively different."

The article also includes at page 332 figures showing the difference in chemical structure between civamide, which is the cis-isomer of capsaicin used in the method of the present invention, and nonivamide. The article goes on to note the "gross errors" that have arisen in both the chemical and pharmaceutical industries and in the chemical literature as a result of this confusion.

As the Examiner has noted, the unpredictability of painful disorders is very high. This unpredictability, coupled with the important but often unrecognized differences between nonivamide and capsaicin and the resulting confusion in the literature, means that the disclosure of "synthetic" capsaicin as an analgesic in the Brand and Lahann references would not suggest to one skilled in the art that civamide would be an effective treatment for painful disorders.

Nor does Brand teach or suggest the long-term effects of treatment as taught and claimed in the present application. Brand teaches that effectiveness retained "up to three days in some cases" is an "unusually long" time period, page 6, lines 9-11. In the present invention, a relatively long period is "at least many weeks" (claim 2), or "at least many weeks or months" (claim 4). As Brand does not teach or suggest the civamide compound recited in the claims, and does not teach or suggest the surprisingly long duration of pain diminishment as recited in the claims, the present application is patentable over the Brand reference.

A Notice of Allowance is respectfully requested.

Respectfully submitted,

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